First Report of Human Granulocytic Ehrlichiosis from Southern Europe (Spain)

To the Editor: Human granulocytic ehrlichiosis (HGE) is a tickborne zoonosis described in the United States several years ago (1) and in Europe recently (2). Several hundred cases have been reported in the United States (3). In Europe, nine cases have been reported, six in Slovenia (2,4-6), and three in Sweden (I. Eliasson, http:\\www.healthnet.org/programs/promed.html). We report a serologically confirmed case of HGE in La Rioja, a Lyme disease-endemic area in northern Spain (7-9).

On August 7, 1999, a 16-year-old man from La Rioja, who had been bitten by a tick 15 days before, was seen in an emergency room and treated with 100 mg of doxycycline twice a day. On August 9, he was hospitalized with a 3-day history of malaise, myalgias, headache, and fever (39ºC). The fever abated in the next 36 hours. The patient had not noticed any signs of inflammation or skin rash, and no signs of neurologic injury were evident. He had abdominal pain when the liver was palpated. Chest radiographs were normal, and abdominal ultrasonography showed no abnormalities. Laboratory studies showed a level leukocyte count (3,001/mm^3 [normal range, 4,500-11,000] with 4.3% band forms, 72.3% neutrophils, 4.7% monocytes, 16.7% lymphocytes, and a platelet count of 114,000/mm^3 [normal, 160,000-410,000]). The hemoglobin level was normal. No inclusions (morulae) suggestive of *Ehrlichia* or *Babesia* spp. were seen on blood smears. The erythrocyte sedimentation rate was normal. The aspartate aminotransferase level was 72 U/L [normal, 5-40]; alanine aminotransferase, 65 U/L [normal, 5-40]; and lactodehydrogenase, 637 U/L [normal, 100-250]. All serologic assays were performed by the same, widely experienced microbiologist, in one laboratory. Serologic test results were negative for *Borrelia burgdorferi* (by enzyme-linked immunosorbent assay [ELISA]); *Rickettsia conorii* (indirect fluorescent-antibody assay [IFA]; *Coxiella burnetti* (IFA); *Ehrlichia chaffeensis* (IFA); the agent of HGE (IFA); and hepatitis A, B, and C viruses (ELISA); and indicated immunity for Epstein-Barr virus. Four weeks later, the aminotransferase levels were normal, and the patient was asymptomatic. A new serum determination showed an HGE antibody titer of 1:64 (HGE IFA IgG MRL Diagnostics, California, USA); the serum tested negative for the other microorganisms tested, including with a new test for *E. chaffeensis*. Another serum sample from the patient taken 8 weeks later showed a titer of 1:256 to the HGE agent. An EDTA-treated sample of whole blood obtained from the patient on day 4 after start of doxycycline treatment was negative for the *E. phagocytophila* genogroup by polymerase chain reaction (PCR). We used a set of primers based on the published sequence of the 16s rNA of *E. phagocytophila* (E1: 5'- GGC ATG TAG GCG GTT CGC TAA GTT - 3' and E2: 5'- CCC CAC ATT CAG CAC TCA TCG TTT A -3') (7). Multiple water samples and a positive blood sample from an experimentally infected lamb were used as controls for PCR amplicon contamination. Doxycycline was administered for 14 days, and the patient's clinical and laboratory abnormalities resolved.

Many tickborne diseases are present in La Rioja. The prevalence of *E. phagocytophila* genogroup in the tick *Ixodes ricinus* is high (24.1% of nymphs, determined by PCR) in La Rioja, and evidence of HGE infection in patients at risk has been reported (10,11). This patient's history of previous tick bite, flulike symptoms, seroconversion to HGE agent, aminotransferase elevation, and response to doxycycline suggest the diagnosis of HGE. As in other reported cases in Europe, no morulae suggestive of *Ehrlichia* infection in the acute phase were visible, the clinical manifestations were moderate, and the fever abated quickly with treatment. Also, as in other cases, the negative PCR result can be explained by the prior treatment with doxycycline.

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